59. (New) The biological preparation of claim 57, wherein said glycosaminoglycans degrading enzyme is selected from the group consisting of a heparanase, a heparinase, a glucoronidase, a heparitinase, a hyaluronidase, a sulfatase and a chondroitinase.

REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-53 are in this case. Claims 9-53 were withdrawn under a restriction requirement as drawn to a non-elected invention. Claims 1-8 have been rejected. Claims 1-53 have now been canceled. New claims 54-59 have now been added.

Following the Interview held with the Examiner, Applicant has chosen (i) to draft two new independent claims, the first (54) being limited to cells, the second (57), to tissues; for both independent claims: (ii) to more clearly emphasize that the biological preparation is an "ex vivo preparation"; (iii) to limit each of the independent claims to the use of a glycosaminoglycans degrading enzyme; and (iv) to more clearly set out the purpose of the external addition of the enzyme, which, as can be interpreted from the Examiners opinion in the previous Action, carries no patentable weight in the context of composition claims.

35 U.S.C. § 102(b) Rejections - Fuks et al.

The Examiner has rejected claims 1 and 6 under 35 U.S.C. § 102(b) as being anticipated by Fuks et al. The Examiner's rejections are respectfully traversed. Claims 1 and 6 have now been canceled, thereby rendering moot the Examiner's rejections with respect to these claims.

The Examiner points out that the specification teaches that the term "externally adhered" refers to -- associated with. New claims 54 and 57 are limited to cells or tissue, respectively. The specification teaches, on page 31, lines 5-11, that the term "externally adhered", when applies to cells or tissues, refers to associated with the extracellular matrix, or, in other words, externally adhered:

> As used herein in the specification and in the claims section below, the term "externally adhered" refers to associated with, e.g., presented. When applies to cells (or tissues) it refers to associated with the extracellular matrix. It will be appreciated that some cells/tissues have inherent extracellular matrix degrading enzyme(s) adhered thereto. The present invention, however, is directed at adding additional adhered enzyme thereto by man intervention.

The Examiner further states that administration of the pharmaceutical composition of Fuks et al. which contains heparanase, a glycosaminoglycans degrading enzyme, results in the formation of a biological material having heparanase externally adhered thereto.

Applicant argues in this respect the following:

First, a biological material having heparanase externally adhered thereto obtained by administering heparanase onto a tissue such as skin in vivo does not constitute patentable subject matter because such a biological material reads on a portion of a human body.

Second, the term "biological preparation" that is recited in the preamble of the independent claims (both canceled claim 1 and new claims 54 and 57) in effect means, as is well accepted in the art, an "ex vivo preparation". It is well known that biological preparations are prepared from cells or tissues that were first removed from a living organisms.

In view of the above it is argued that canceled claim 1 and new claims 54 and 57 do not read, and should not be interpreted as reading, on "in vivo biological material having heparanase externally adhered thereto", which, as stated above, is not patentable subject matter, and therefore these claims are clearly not anticipated by Fuks et al.

In order to further clarify this issue, Applicant has chosen to add to new independent claims 54 and 57 the recitation "ex vivo", so as to render clearer the fact that the claimed biological preparation is not an "in vivo biological preparation". This recitation does not add new searchable subject matter to the claims because, as is already stated above, it is well known that biological preparations are prepared from cells or tissues that were first removed from a living organisms.

Thus, Fuks et al. fails to teach a biological preparation for use in vivo comprising, ex vivo, cells or tissues and a purified, natural or recombinant, glycosaminoglycans degrading enzyme externally adhered thereto and therefore fails to anticipate new claims 54 and 57.

It is therefore the Applicant's strong opinion that the present invention as claimed is not anticipated, nor is it rendered obvious by the teachings of Fuks et al.

It is thus the Applicant's opinion that claims 54 and 57 are allowable, rendering claims 55-56 and 58-59, which depend therefrom, also allowable.

35 U.S.C. § 102(b) Rejections - Sigma Catalog

The Examiner has rejected claims 1, 2, 4 and 7 under 35 U.S.C. § 102(b) as being anticipated by the Sigma Catalog. The Examiner's rejections are respectfully traversed. Claims 1, 2, 4 and 7 have now been canceled, thereby rendering moot the Examiner's rejections. New claims 54-59 have now been added.

The Examiner points out that Sigma sells and teaches the use of collagenase for the hydrolysis of native collagen in the isolation of cells from animal tissue and tissue culture.

New claims 54-59 are limited to the use of a glycosaminoglycans degrading enzyme. Collagenase, is not a glycosaminoglycans degrading enzyme as it degrades collagen, a protein.

It is being emphasized in this respect that the "glycosaminoglycans degrading enzyme" limitation was already searched in context of now canceled claims 7 and 8.

Therefore, new claims 54-59 are not anticipated, nor are they rendered obvious by the Sigma Catalog and are therefore allowable.

35 U.S.C. § 103(a) Rejections - Fuks et al. and Wang et al.

The Examiner has rejected claims 1-5, 7 and 8 under 35 U.S.C. § 103(a) as being unpatentable over Fuks et al. and Wang et al. The Examiner's rejections are respectfully traversed. Claims 1-5, 7 and 8 have now been canceled. New claims 54-59 have now been added.

In the previous Action, the Examiner pointed out that both Fuks et al. and Wang et al. teach that heparanase, while degrading extracellular matrix in vivo, releases therefrom factors which can assist in various healing processes and even name some of them. This function of heparanase is well known to the Applicants as is evident from the background section of the instant application.

However, the present invention as claimed uses the extracellular matrix degrading activity of heparanase or other glycosaminoglycans degrading enzymes ex vivo. Such an ex vivo use results in depletion of the factors from the claimed biological preparation which are released to the ex vivo medium and is therefore not at all in line with the motivation resulting from the teachings of Fuks et al. and

Wang et al. Based on the teachings of Fuks et al. and Wang et al. one ordinarily skilled in the art would be motivated to add heparanase in vivo so as to cause the release of the beneficiary growth factors thereat. Based on the teachings of Fuks et al. and Wang et al., however, one ordinarily skilled in the art would not be motivated to add heparanase ex vivo because such addition would results in the reverse action, i.e., depletion of the factors from the biological preparation. Based on the teachings of Fuks et al. and Wang et al. one ordinarily skilled in the art would be motivated to administer, in situ, in vivo, larger amounts of heparanase as is compared to the amount thereof adherable ex vivo to cells or tissues, so as to maximize the beneficiary effect of releasing growth factors from the extracellular matrix.

It is, therefore, the Applicant's opinion that claims 54-59 are not rendered obvious by the teachings of Fuks et al. and Wang et al. because these teachings fail to create a motivation to treat an implant ex vivo with a glycosaminoglycans degrading enzyme, because the result of such a treatment would be depletion of growth factors therefrom.

Applicant therefore strongly argues that claims 54-59 are allowable.

35 U.S.C. § 103(a) Rejections - Sigma Catalog

The Examiner has rejected claims 3 and 5 under 35 U.S.C. § 103(a) as being unpatentable over the Sigma Catalog. The Examiner's rejections are respectfully traversed. Claims 3 and 5 have now been canceled, thereby rendering moot the Examiner's rejections. New claims 54-59 have now been added.

New claims 54-59 are limited to the use of a glycosaminoglycans degrading enzyme. Collagenase, is not a glycosaminoglycans degrading enzyme as it degrades collagen, a protein.

It is being emphasized in this respect that the "glycosaminoglycans degrading enzyme" limitation was already searched in context of now canceled claims 7 and 8.

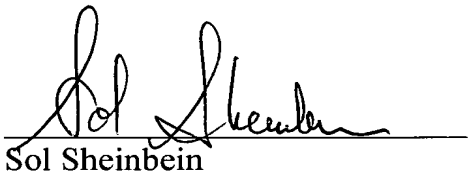
Therefore, new claims 54-59 are not rendered obvious by the Sigma Catalog and are therefore allowable.

Limitations and recitations recited is new claims 54-59

Independent claim 54 is limited to cells and independent claim 57 is limited to a tissue or a tissue portion. These limitations were searched with respect to canceled claims 2 and 4. The independent claims are limited by the term "ex vivo". This limitation was searched because biological preparations are inherently "ex vivo" and further because a claim should not be interpreted as relating to a non-patentable subject matter -- an in vivo biological preparation (in human). The independent claims are limited to the use of a glycosaminoglycans degrading enzyme, which limitation was searched with respect to canceled claims 7 and 8. The "so as to enhance extravasation, implantation, transplantation, invasion and/or migration of said cells in vivo" recitation of claim 54 and the "so as to enhance implantation of said tissue or said tissue portion in vivo" recitation of claim 57 carry, as can be interpreted from the Examiner statements in the previous Action, no patentable weight with respect to composition claims and therefore need not be searched. These recitations find ample support in the specification, see, for example, pages 9-15 for "implantation" and "transplantation", pages 5 and 14 for "migration" and "invasion"; and pages 4 and 16 for "extravasation".

In view of the above amendments and remarks it is respectfully submitted that claims 54-59 are now in condition for allowance. Prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,



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